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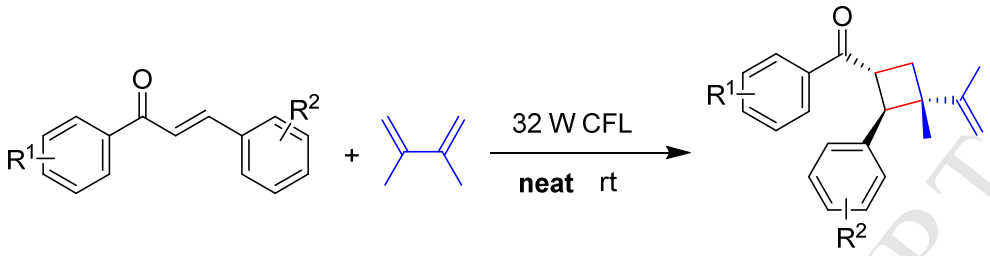
Graphical Abstract



neat reaction conditions
DFT studies supported mechanism

up to 72% yield

The visible-light-promoted intermolecular [2+2] cycloaddition of chalcones with 2,3-dimethyl-1,3-butadiene for the synthesis of cyclobutane derivatives is described.

Intermolecular [2+2] photocycloaddition of chalcones with 2,3-dimethyl-1,3-butadiene under neat reaction conditions

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Abstract: The intermolecular [2+2] photocycloaddition of chalcones with 2,3-dimethyl-1,3-butadiene under visible-light irradiation for the synthesis of cyclobutane derivatives has been developed. Without using any photosensitizer, metallic catalyst and solvent, the reaction proceeded with high regioselectivity and moderate to high stereoselectivity. Mild reaction conditions and no additives make the reaction easy to operate. Control experiments and density functional theory (DFT) computations demonstrated that the reaction takes place via visible-light activation of chalcones, which is different from the previously reported [2+2] cycloaddition of chalcones.

Key words: visible-light, [2+2] cycloaddition, solvent- and catalyst-free, cyclobutane derivatives, chalcone, 2,3-dimethyl-1,3-butadiene

1. Introduction

As fossil-fuel energy resources are shrinking rapidly and air pollution is getting worse, it is urgent to seek and utilize energy sources that are sustainable and environmentally friendly.[1] Visible-light as a clean, cheap, and endlessly renewable energy source has drawn significant attention from chemists.[2] Photochemical reactions can enable the formation of special molecular structures that are usually difficult to accomplish by traditional means.[3] Photochemical substrates can be activated by light without additional reagents, which reduces the generation of byproducts, making it attractive in green synthetic chemistry.[2a] Cyclobutane subunits occur in a large amount

of complex natural products,[4] and cyclobutanes are important intermediates for the synthesis of many organic compounds.[5] The ring strain of a four-membered ring makes it easy to be opened or expanded to a larger ring system.[6] Thus, the research on the construction of cyclobutane backbones is an indispensable part of organic synthesis.[7] One of the most synthetically direct and common methods is a photochemical [2+2] cycloaddition reaction. In addition to ultraviolet (UV) which is traditionally used to promote [2+2] cycloaddition, visible-light is also an effective means for the construction of four-membered ring compounds.[6, 8] Visible-light is more easily available than UV and it has advantages when used for the synthesis of compounds that are sensitive to photodegradation under UV irradiation. Because of these features, visible-light has a broader range of applications than UV in organic synthesis.[9]

Chalcones are naturally occurring α,β-unsaturated carbonyl compounds[10] widely distributed in plants. Due to the convenience of synthesis, a large number of chalcone derivatives have been prepared. Many natural and synthetic chalcones have been demonstrated to exhibit various biological activities.[11] For example, methyl chalcone has been sold as an essential oil, and sofalcone has been used as a mucosal protective drug.[12] Therapeutic application of chalcones can be traced back thousands of years by using herbs to treat different diseases.[11b, 13]

The cycloaddition of α,β-unsaturated carbonyl compounds with olefins is an important type of reaction for the construction of cyclobutanes. However, relatively few works have been reported on the intermolecular [2+2] cycloaddition of chalcones with olefins. In 2016, Yoon and coworkers reported a chiral Lewis acid complex-catalyzed triplet energy transfer from an electronically excited photosensitizer, and they applied this strategy to enantioselective [2 + 2] photocycloadditions of 2'-hydroxychalcones by using $Ru(bpy)_3(PF_6)_2$ as a sensitizer, in which Lewis acid coordination lowers the triplet energy of the chalcone substrate.[14] In 1998, Toda and coworkers reported the intermolecular [2+2] cycloaddition of chalcones in the molten state irradiated by a 400 W high-pressure Hg lamp.[15a] In 2017, Wu and coworkers reported the intermolecular [2+2] cycloaddition of chalcones and cinnamic acid derivatives in dichloroethane, using *fac*-tris(2-phenylpyridinato-C_2,N) iridium as a photosensitizer, in which triplet chalcones and cinnamic acid derivatives were produced by energy transfer.[15b]

Herein, we report the intermolecular [2+2] cycloaddition of chalcones with 2,3-dimethyl-1,3-butadiene for the synthesis of functionalized cyclobutanes under the irradiation of visible-light at room temperature under neat reaction conditions. The corresponding products were obtained in yields of up to 72% with high regioselectivity and moderate to high stereoselectivity. Mild reaction conditions and no additives make the reaction easy to operate. Control experiments and density functional theory (DFT) computations demonstrated that the reaction takes place via visible-light activation of chalcones.

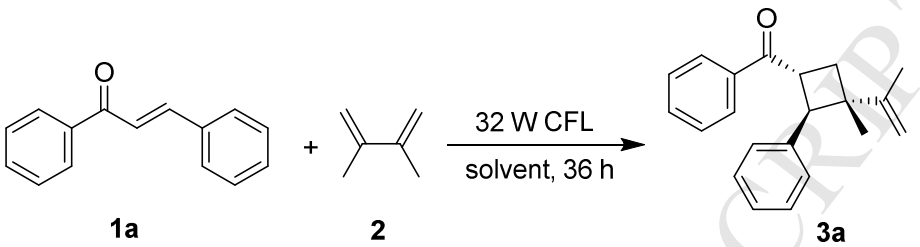
2. Results and discussion

Initially, the model reaction of chalcone (**1a**, 0.3 mmol) with 2,3-dimethyl-1,3-butadiene (**2**, 1.0 mmol) was performed at room temperature under irradiation of a 32 W compact fluorescent light (CFL) bulb. Several commonly used solvents were screened, and the results are shown in **Table 1.** The data indicated that the model [2+2] cycloaddition reaction was remarkably influenced by solvent. Product **3a** was obtained in the best yield of 33% when using methanol as a solvent (**Table 1**, entry 1). Only a trace amount of product was obtained in THF or CH_2Cl_2 (**Table 1**, entries 6 and 7). Using acetonitrile/methanol (1:3) as a mixed solvent gave the product in a 30% yield (**Table 1**, entry 8). Since 2,3-dimethyl-1,3-butadiene (**2**) is a liquid, we postulated that if **2** can dissolve chalcone (**1a**), the solvent may not be necessary. In order to test our hypothesis, an experiment was implemented without any solvent under neat reaction conditions. Much to our delight, the desired product **3a** was obtained in 72% yield. The yield is better, compared to the reaction with CH_3OH as a solvent at the same reaction time (**Table 1**, entries 10 and 11). Hence, all the reactions were performed under neat reaction conditions.

We speculate that the photocycloaddition reaction was significantly affected by solvent probably due to the following possible causes: Solvent affects the triplet lifetime of chalcone (it has been reported that solvent has effect on the triplet lifetime of some rhodamine dyes[16]). Solvent may also affect the rates of 1,4-diradical intermediates (**Scheme 4**) reversing back to the starting materials and converting forward to the products.[18d] Moreover, it is believed that photochemical reactions of α,β-unsaturated carbonyl compounds occur from the lowest-lying triplet state T_1

(**Scheme 4**), which is often of ππ* character. However, the energy difference between the nπ* and the ππ* triplet state in these compounds is relatively small. Thus, the character of the T_1 state is variable and can be affected by solvent polarity[7a].

Table 1. Solvent screening [a]



entry	solvent	yield (%)[b]	dr[e]
1	methanol	33	4.7:1
2	*i*-PrOH	22	4.0:1
3	acetone	13	4.2:1
4	MeCN	10	4.9:1
5	DMSO	7	5.2:1
6	THF	trace	-
7	CH_2Cl_2	trace	-
8	MeCN/MeOH (1:3)	30	5.0:1
9	MeCN/*i*-PrOH (1:3)	22	5.0:1
10[c]	CH_3OH	64	4.7:1
11[d]	none	72	4.0:1

[a] Unless otherwise noted, reaction conditions: **1a** (0.3 mmol), **2** (1.0 mmol), solvent (2.0 mL), under irradiation of a 32 W CFL at rt for 36 h. [b] Isolated yield. [c] **1a** (0.3 mmol), **2** (1.36 mL), CH_3OH (2.0 mL).[d] **1a** (0.3 mmol), **2** (1.36 mL). [e] dr was determined by ^1H NMR analysis.

After optimizing the reaction conditions with chalcone (**1a,** 0.3 mmol) and commercially available 2,3-dimethyl-1,3-butadiene (**2**) as a model system, the best yield of 72% was obtained when using 1.36 mL of **2** under the irradiation of a 32 W CFL (For details, please see the **Supporting Information (SI) Table S1**).

With the optimal conditions in hand, we investigated the substrate scope of the intermolecular [2+2] photocycloaddition reaction. A variety of chalcones were synthesized and subjected to the reaction conditions, as shown in **Scheme 1.** The reactions led to the desired products in 27% to 72%

yields. It can be seen that substituent groups had significant effects on the reaction. For example, chalcones with an alkenyl benzene ring bearing either an electron-donating (-Me, -OMe) or an electron-withdrawing (-Cl, -Br) group gave good yields (**3b**, **3c**, **3e** and **3f**). However, the yield was obviously decreased for the chalcone bearing two -Cl on alkenyl benzene ring (**3d**), probably due to the influence of both steric and electronic effects. The chalcones with an electron-donating group (-Me or -OMe) on carbonyl aromatic ring gave higher yields (**3h**-**3k**) than those with an electron-withdrawing group (-NO_2) (**3g**). The chalcone substituted by -OMe at the *ortho* position of the carbonyl aromatic ring (**3i**) provided a better yield than those substituted by -OMe at the *meta* position (**3j**) and *para* position (**3k**). Additionally, the benzalacetone was investigated as a substrate, and a moderate yield (**3l)** was obtained under the same reaction conditions. Isoprene can also participate in the reaction, and the desired product (**3m**) was obtained in 54% yield (**Scheme 2**). However, pent-1-en-3-one, butyl acrylate, ethyl cinnamate etc resisted participating in the reaction (for details, please see **SI**, **Scheme S1**). It is worth mentioning that all the products are new compounds. Among the investigated reactions, four of them showed excellent diastereoselectivity (Only single diastereomer was observed by ^{1}H NMR, dr >20:1). The others gave the products as a mixture of diastereomers. We have tried to isolate them by flash column chromatography, prep-TLC and HPLC (with InertSustain C18 column), but failed. ^{1}H NMR indicated that there are two major diastereomers with dr ranged from 2:1 to 6:1; the major diastereomers (**3a** – **3h** and **3m**) can be isolated by recrystallization after column chromatography. The relative configuration of product **3a** was unambiguously determined by single-crystal X-ray diffraction analysis (**Figure 1**). The relative configurations of other products **3** (**3b** – **3m**, the major diastereomers) were assigned by analogy.

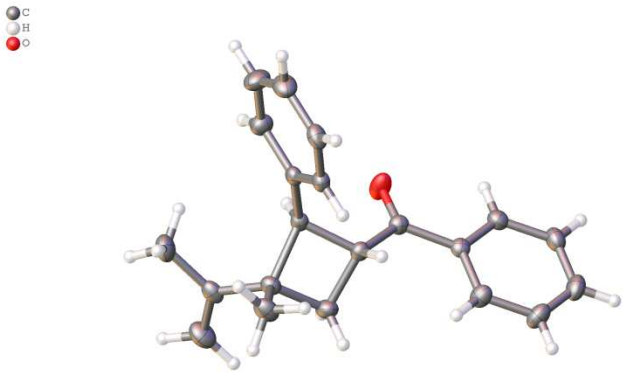
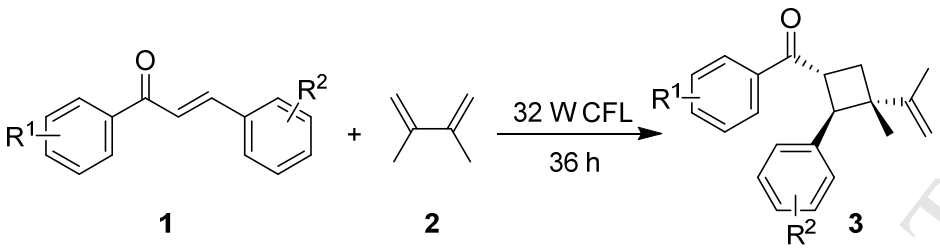
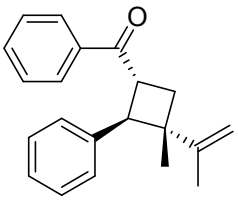


Figure 1 Single-crystal X-ray diffraction analysis of **3a**

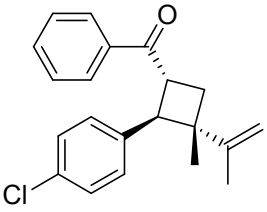
Scheme 1. Substrate scope [a]



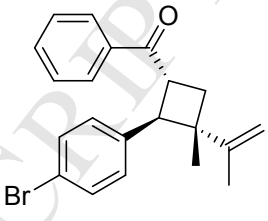
1 **2** **3**



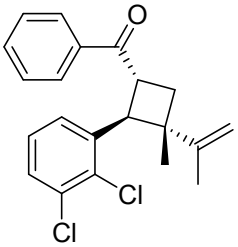
3a
72% 4:1 dr



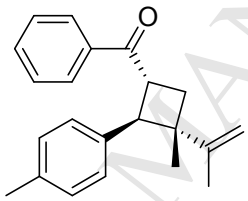
3b
63% 4:1 dr



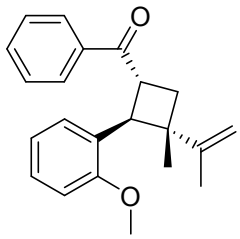
3c
63% 2:1 dr[b]



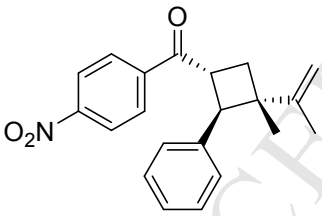
3d
31% 3:1 dr[b]



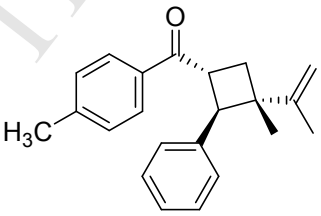
3e
61% 2:1 dr[b]



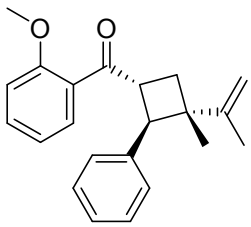
3f
49% 6:1 dr



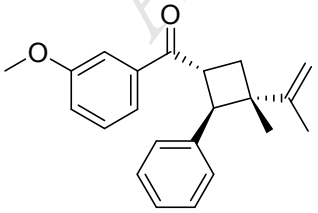
3g
27% 3:1 dr



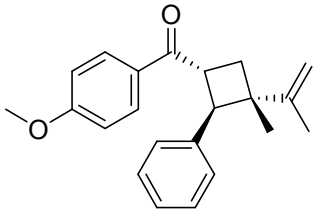
3h
58% 4:1 dr[b]



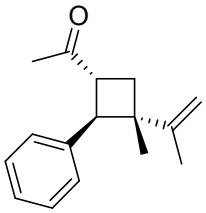
3i
60% >20:1 dr



3j
54% >20:1 dr



3k
45% >20:1 dr

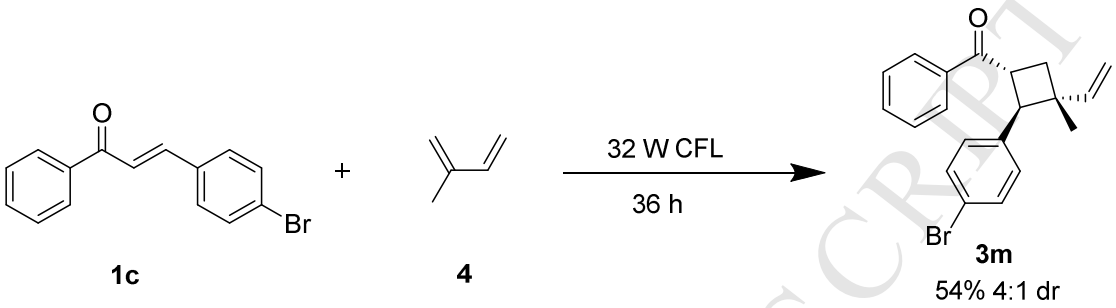


3l
41% >20:1 dr

[a] Reaction conditions: **1** (0.3 mmol) and **2** (1.36 mL) under irradiation of a 32 W CFL at rt for 36 h. Yield of the isolated product (the average of two repetitions).

[b] The ratio of two major diastereoisomers.

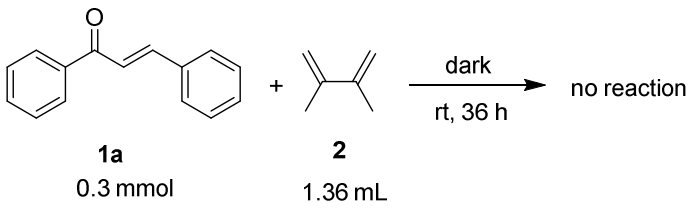
Scheme 2. The photocycloaddition between chalcone 1c and isoprene [a]



[a] Reaction conditions: **1c** (0.3 mmol) and isoprene **4** (0.9 mL) under irradiation of a 32 W CFL at rt for 36 h. Yield of the isolated product.

To understand the reaction mechanism, a control experiment was conducted (**Scheme 3**). No reaction was observed for the experiment run in the dark at room temperature, indicating that light is indispensable. We then measured the UV-visible absorption of chalcone (**1a**), 2,3-dimethyl-1,3-butadiene (**2**) and the mixture of **1a** and **2**. It was found that **1a** had a strong absorption between 400-430 nm at 2.2×10^{-2} mol/L while **2** did not show any absorption in the visible range, and addition of **2** had no obvious effect on the absorption of **1a** (For the absorption spectra, please see the **SI**, **Figure S1-S3**). These results demonstrated that chalcone can absorb energy from visible-light (The emission spectra range of CFL has been reported as 400-720 nm[17]) to promote the reaction.

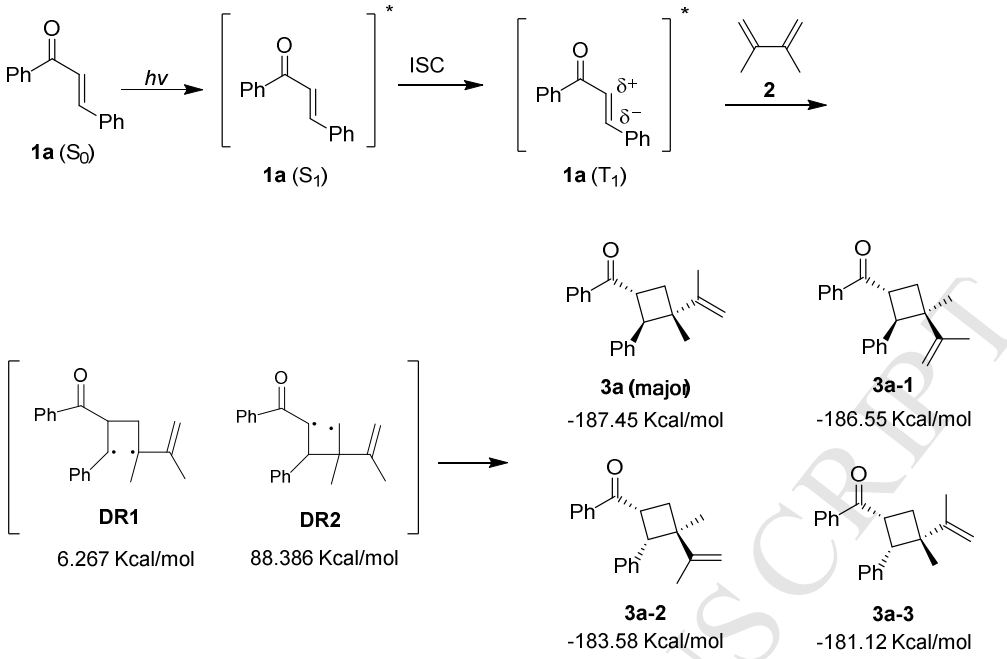
Scheme 3 The control experiment



On the basis of the control experiment, and previously researched works[18], a possible reaction mechanism was proposed (**Scheme 4**). Under visible-light irradiation, chalcone molecules (**1a**) absorb photons to be excited from ground state (S_0) to the first excited singlet state (S_1), and then, S_1 undergoes a rapid intersystem crossing (ISC) to form the excited triplet state (T_1).[19] It has been demonstrated that the π^* of the enone triplet state is occupied by an electron, making the α-position electrophilic and the β-position nucleophilic[18d, 20], meaning that the excitation induces the umpolung of the enone. Thus, when it reacts with olefins bearing electron-donating groups, head-to-tail (HT) products are generated. On the contrary, when it reacts with olefins containing electron-withdrawing groups, head-to-head (HH) products are produced.[11b] In this reaction, the excited triplet state (T_1) of chalcone goes through the HT intermolecular cycloaddition with 2,3-dimethyl-1,3-butadiene (**2**) to generate 1,4-diradical intermediates[21] (**DR1** and **DR2**), which undergo ring closure to generate the cyclobutane **3**.[21]

To further verify the mechanism, we conducted density function theory (DFT) calculations. The energy barrier between the substrates and transition state for **DR1** is 6.267 Kcal/mol, and for **DR2** is 88.386 Kcal/mol. Obviously, **DR1** is easier to generate than **DR2**, suggesting that **DR1** is the main 1,4-diradical intermediate. According to this mechanism, the product can be formed with four relative configurations (**3a** – **3a-3**). The DFT calculations indicated that **3a** has the lowest energy (-187.45 Kcal/mol relative to substrates) among the four possible diastereomers, suggesting that **3a** is the main product (For details about the DFT calculations, please see the SI). This is completely consistent with the experimental results.

Scheme 4 Proposed reaction mechanism



3. Conclusion

In summary, we have developed a visible-light promoted intermolecular [2+2] cycloaddition reaction of chalcones with 2,3-dimethyl-1,3-butadiene under neat reaction conditions at room temperature. The corresponding cyclobutane derivatives were synthesized with yields of up to 72%. Mild reaction conditions and no additives make the reaction easy to operate. Control experiments and DFT computations demonstrated that the reaction takes place by visible-light activing chalcones. This work provides a convenient and gentle method for the preparation of cyclobutanes.

4. Experimental section

4.1. General

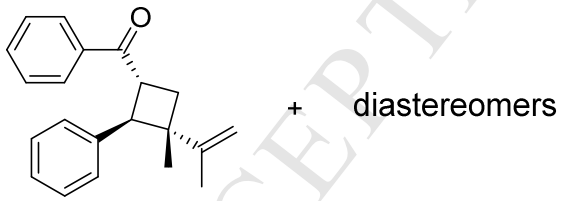
trans-Chalcone (**1a**) was purchased from Alfa Aesar, A Johnson Matthey Company. 2,3-Dimethyl-1,3-butadiene was purchased from Energy Chemical. Unless otherwise noted, all reagents were purchased from commercial suppliers and used without further purification. α,β-Unsaturated ketones (**1b-1k**) were prepared according to literatures[22] (for details, please see SI). Reactions were monitored by thin-layer chromatography (TLC) with GF254 silica gel plates using UV light and vanillic aldehyde as visualizing agents. Flash column chromatography was performed using 200-300 mesh silica gel. ^{1}H NMR and ^{13}C NMR spectra were recorded on

Bruker-AM 600 (600 MHz). Chemical shifts were reported in ppm from TMS with the solvent resonance as the internal standard. Data were reported as follows: chemical shifts (δ) in ppm, coupling constants (*J*) in Hz, and solvent ($CDCl_3$ and DMSO-d_6). High-resolution mass spectra were obtained by using ESI ionization sources (Varian 7.0 T FTICR-MS). Melting points were taken on a WPX-4 apparatus and were uncorrected. Emission spectra were taken on HITACHI F-7000 fluorescence spectrophotometer.

4.2. General procedure for the intermolecular [2+2] photocycloaddition

A round-bottom flask was charged with *trans*-chalcone (**1**) (0.3 mmol), 2,3-dimethyl-1,3-butadiene (**2**) (1.36 mL). The resultant mixture was stirred at rt under irradiation of a 32 W CFL, and the reaction was monitored by TLC. The reaction mixture was concentrated *in vacuo*. The residue was purified by silica gel column chromatography with petroleum ether/ethyl acetate (400:1-50:1) as an eluent to give the products **3**. The single diastereomers of **3a-3e** and **3m** were obtained by further recrystallization from products **3** using the mixed solvents of dichloromethane and petroleum ether at rt. The single diastereomer of **3h** was obtained from recrystallization at 4 ^{o}C.

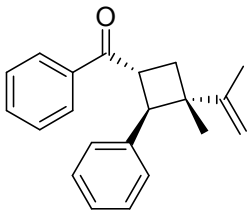
4.2.1. (3-methyl-2-phenyl-3-(prop-1-en-2-yl)cyclobutyl)(phenyl)methanone **(3a)**



3a (major)

3a (major) and diastereomers as a mixture: Yield (62.5 mg, 72%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.93 (d, *J* = 7.4 Hz, 1.41H), 7.59 (d, *J* = 7.3 Hz, 0.36H), 7.53 (t, *J* = 7.4 Hz, 0.78H), 7.43 (t, *J* = 7.7 Hz, 1.43H), 7.28 (t, *J* = 7.6 Hz, 1.61H), 7.24 – 7.17 (m, .33H), 6.98 – 6.92 (m, 0.78H), 4.89 (s, 0.72H), 4.83 (s, 0.17H), 4.82 (s, 0.67H), 4.75 (s, 0.16H), 4.43 (dd, *J* = 18.2, 10.0 Hz, 0.18H), 4.21 (dd, *J* = 18.6, 9.3 Hz, 0.82H), 4.16 (d, *J* = 9.7 Hz, 0.68H), 3.71 (dd, *J* = 9.8, 2.5 Hz, 0.18H), 3.33 (t, *J* = 11.1 Hz, 0.21H), 2.36 (t, *J* = 10.0 Hz, 0.82H), 2.22 – 2.16 (m, 0.76H), 2.11 – 2.05 (m, 0.20H), 1.74 (s, 2.23H), 1.62 (s, 0.58H), 1.16 (s, 2.08H), 1.14 (s, 0.59H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 200.3, 152.4, 149.7, 140.0,

136.2, 133.0, 132.3, 128.8, 128.6, 128.4, 128.1, 128.1, 128.0, 127.8, 127.4, 126.3, 126.1, 110.7, 108.9, 57.5, 47.9, 46.2, 45.0, 42.2, 41.0, 36.4, 32.1, 29.7, 21.9, 18.8, 18.4.

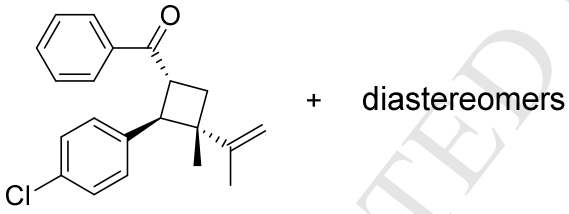


3a

White solid, mp 103 – 105 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.99 (d, *J* = 7.7 Hz, 2H), 7.62 (t, *J* = 7.3 Hz, 1H), 7.50 (t, *J* = 7.5 Hz, 2H), 7.31 (q, *J* = 7.7 Hz, 4H), 7.21 (t, *J* = 6.6 Hz, 1H), 4.80 (d, *J* = 29.2 Hz, 2H), 4.57 (q, *J* = 9.4 Hz, 1H), 3.91 (d, *J* = 9.8 Hz, 1H), 2.21 – 2.10 (m, 2H), 1.69 (s, 3H), 1.09 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 200.3, 152.4, 140.0, 136.2, 133.0, 128.6, 128.4, 128.1, 128.1, 126.3, 108.9, 47.9, 45.0, 41.0, 36.4, 21.9, 18.8.

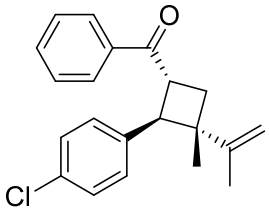
HRMS (ESI) calc. for $C_{21}H_{22}O$ $(M+Na)^+$: 313.1563, found: 313.1568.

4.2.2. (2-(4-chlorophenyl)-3-methyl-3-(prop-1-en-2-yl)cyclobutyl)(phenyl)methanone **(3b)**



3b (major)

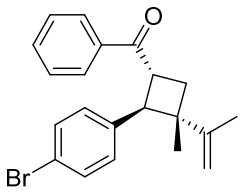
3b (major) and diastereomers as a mixture: Yield (61.4 mg, 63%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.92 (d, *J* = 7.4 Hz, 1.59H), 7.83 (d, *J* = 7.5 Hz, 0.41H), 7.55 (t, *J* = 7.4 Hz, 0.81H), 7.52 – 7.49 (m, 0.21H), 7.44 (t, *J* = 7.7 Hz, 1.59H), 7.42 – 7.37 (m, 0.53H), 7.25 – 7.22 (m, 2.10H), 7.19 (d, *J* = 8.5 Hz, 0.32H), 7.17 – 7.10 (m, 2.00H), 5.00 (s, 0.13H), 4.94 (s, 0.17H), 4.86 (s, 0.83H), 4.82 (s, 0.83H), 4.18 – 4.12 (m, 1.65H), 3.98 – 4.02 (m, 0.17H), 3.65 (d, *J* = 8.4 Hz, 0.14H), 2.82 – 2.75 (m, 0.19H), 2.34 – 2.32 (m, 0.85H), 2.25 – 2.23 (m, 0.29H), 2.23 – 2.18 (m, 0.84H), 1.73 (s, 2.44H), 1.67 (s, 0.44H), 1.39 (s, 0.39H), 1.14 (s, 2.76H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 200.0, 152.1, 147.9, 139.2, 138.6, 136.0, 135.8, 133.1, 133.1, 132.2, 130.4, 129.4, 129.2, 128.8, 128.6, 128.6, 128.4, 128.2, 128.0, 111.2, 109.1, 52.2, 47.1, 45.0, 42.4, 41.1, 37.0, 36.6, 33.9, 28.6, 21.8, 20.2, 18.8.



3b

White solid, mp 118 – 120 ^{o}C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.98 (d, *J* = 7.4 Hz, 2H), 7.63 (t, *J* = 7.4 Hz, 1H), 7.51 (t, *J* = 7.7 Hz, 2H), 7.36 (s, 4H), 4.81 (s, 1H), 4.78 (s, 1H), 4.57 (q, *J* = 9.5 Hz, 1H), 3.90 (d, *J* = 9.8 Hz, 1H), 2.20-2.17 (m, 1H), 2.14 – 2.10 (m, 1H), 1.67 (s, 3H), 1.08 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 200.6, 152.8, 139.1, 133.8, 131.5, 130.7, 129.2, 128.8, 128.4, 109.1, 47.5, 45.0, 40.3, 36.1, 21.7, 19.0. HRMS (ESI) calc. for $C_{21}H_{21}ClO$ $(M+Na)^{+}$: 347.1173, found: 347.1172.

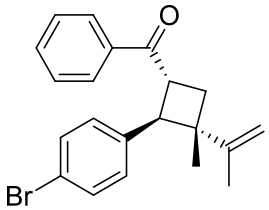
4.2.3. (2-(4-bromophenyl)-3-methyl-3-(prop-1-en-2-yl)cyclobutyl)(phenyl)methanone **(3c)**



+ diastereomers

3c (major)

3c (major) and diastereomers as a mixture: Yield (69.8 mg, 63%); ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.98 (d, *J* = 7.4 Hz, 0.97H), 7.92 – 7.87 (m, 0.81H), 7.78 (d, *J* = 7.5 Hz, 0.22H), 7.65 – 7.56 (m, 1.06H), 7.53 – 7.44 (m, 3.47H), 7.40 (d, *J* = 8.3 Hz, 0.24H), 7.32 (d, *J* = 8.4 Hz, 0.33H), 7.29 (d, *J* = 8.4 Hz, 0.97H), 7.24 – 7.20 (m, 0.81H), 7.17 (d, *J* = 8.3 Hz, 0.23H), 5.05 (s, 0.25H), 5.01 (s, 0.12H), 4.89 (s, 0.23H), 4.86 (s, 0.13H), 4.81 (s, 0.48H), 4.78 (s, 0.49H), 4.56 (q, *J* = 9.5 Hz, 0.51H), 4.22 – 4.17 (m, 0.35H), 3.89 (d, *J* = 9.8 Hz, 0.48H), 3.62 (d, *J* = 8.6 Hz, 0.26H), 2.19 (t, *J* = 9.9 Hz, 0.63H), 2.12 (t, *J* = 10.0 Hz, 0.68H), 2.05 – 2.01 (m, 0.3H), 1.69 (s, 0.3H), 1.68 (s, 1.46H), 1.64 (s, 0.42H), 1.63 (s, 0.44H), 1.32 (s, 0.70H), 1.11 (s, 0.8H), 1.08 (s, 1.4H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 203.2, 200.6, 200.4, 152.8, 147.3,144.8, 140.2, 139.5, 139.2, 135.9, 135.7, 133.8, 133.7, 131.7, 131.5, 131.4, 131.3, 131.2, 131.0, 130.5, 130.2, 129.2, 129.2, 128.8, 128.8, 128.5, 128.3, 125.6, 124.2, 120.1, 120.0, 119.3, 115.1, 113.9, 112.2, 109.1, 51.8, 47.6, 46.6, 46.4, 45.0, 42.6, 41.5, 40.3, 37.9, 37.0, 36.6, 36.1, 34.2, 28.8, 21.7, 21.2, 20.5, 19.0, 18.8

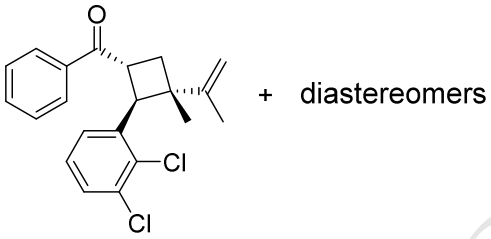


3c

White solid, mp123–125 ^{o}C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.98 (d, *J* = 7.2 Hz, 2H), 7.62 (t, *J* = 7.4 Hz, 1H), 7.51 – 7.48 (m, 4H), 7.29 (d, *J* = 8.4 Hz, 2H), 4.80 (s, 1H), 4.77 (s, 1H), 4.56 (q, *J* = 9.5 Hz, 1H), 3.88 (d, *J* = 9.8 Hz, 1H), 2.16-2.19 (m, 1H), 2.12-1.09 (m, 1H), 1.67 (s, 3H), 1.08 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 205.4, 157.5, 144.3, 140.6, 138.6, 136.1, 135.8, 134.0, 133.6, 124.7, 113.8, 52.3, 49.7, 45.0, 40.9, 26.4, 23.8.

HRMS (ESI) calc. for $C_{21}H_{21}BrO$ $(M+H)^+$: 391.0668, found: 391.0665.

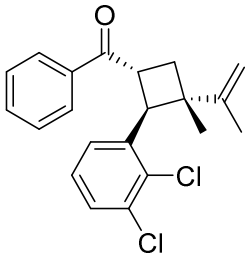
4.2.4. (2-(2,3-dichlorophenyl)-3-methyl-3-(prop-1-en-2-yl)cyclobutyl)(phenyl)methanone **(3d)**



3d (major)

3d (major) and diastereomers as a mixture: Yield (33.4 mg, 31%); Yellow liquid ; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.91 (d, *J* = 7.7 Hz, 0.59H), 7.86 (d, *J* = 7.7 Hz, 0.75H), 7.73 (d, *J* = 7.8 Hz, 0.36H), 7.60 (d, *J* = 7.7 Hz, 0.3H), 7.54 (t, *J* = 7.4 Hz, 0.72H), 7.44 – 7.42 (m, 1.36H), 7.38 – 7.35 (m, 0.48H), 7.33 – 7.31 (m, 0.47H), 7.27 (d, *J* = 7.6 Hz, 0.26H), 7.24 – 7.18 (m, 0.89H), 7.13 (t, *J* = 7.9 Hz, 0.43H), 7.10 (d, *J* = 8.0 Hz, 0.19H), 7.05 (t, *J* = 7.4 Hz, 0.33H), 7.00 – 6.99 (m, 0.34H), 6.98 – 6.94 (m, 0.43H), 6.90 (t, *J* = 8.0 Hz, 0.16H), 5.04 (s, 0.35H), 5.01 (s, 0.39H), 4.97 (s, 0.18H), 4.94 (s, 0.54H), 4.83 (s, 0.14H), 4.76 (s, 0.15H), 4.59 (d, *J* = 10.1 Hz, 0.14H), 4.46 – 4.42 (m, 0.53H), 4.22 – 4.19 (m, 0.16H), 4.09 – 4.05 (m, 0.56H), 3.33 – 3.28 (m, 0.15H), 3.15 – 3.12 (m, 0.18H), 3.08 – 3.05 (m, 0.18H), 2.82 – 2.74 (m, 0.60H), 2.56 – 2.52 (m, 0.23H), 2.22 – 2.19 (m, 0.44H), 2.11 – 2.07 (m, 0.39H), 1.91 (s, 0.14H), 1.78 (s, 0.54H), 1.67 (s, 1.64H), 1.66 (s, 0.43H), 1.50 (s, 1.16H), 1.13 (s, 0.34H), 1.12 (s, 1.06H).^{13}C NMR (150 MHz, $CDCl_3$) δ 199.6, 148.7, 147.4, 142.2, 140.5, 139.6, 136.9, 135.8, 133.4, 133.1, 133.0, 132.9, 132.7, 120.0, 128.7, 128.6, 128.6, 128.4, 128.3, 128.2, 128.2, 128.1, 128.1, 127.7,

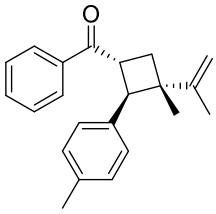
127.2, 127.2, 127.0, 126.7, 126.6, 126.3, 125.6, 124.2, 115.2, 113.1, 111.3, 110.9, 51.7, 48.3, 48.2, 46.7, 46.4, 44.1, 41.6, 41.6, 37.6, 37.4, 37.0, 34.2, 32.4, 29.8, 28.8, 21.0, 20.0, 18.7, 18.6, 18.1.



3d

^{1}H NMR (600 MHz, DMSO-d_6) δ 7.98 (d, *J* = 7.4 Hz, 2H), 7.75 (d, *J* = 7.8 Hz, 1H), 7.64 (t, *J* = 7.4 Hz, 1H), 7.53 – 7.50 (m, 3H), 7.37 (t, *J* = 7.9 Hz, 1H), 4.75 – 4.69 (m, 3H), 4.40 (d, *J* = 9.9 Hz, 1H), 2.33 (t, *J* = 10.0 Hz, 1H), 2.12 (t, *J* = 10.1 Hz, 1H), 1.76 (s, 3H), 1.16 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 200.2, 151.2, 140.0, 135.7, 133.9, 132.4, 131.8, 129.5, 129.2, 129.2, 128.8, 128.0, 110.0, 45.6, 45.3, 41.1, 34.8, 21.5, 19.6. HRMS (ESI) calc. for $C_{21}H_{20}Cl_2O$ $(M+Na)^+$: 381.0783, found: 381.0782.

4.2.5. (3-methyl-3-(prop-1-en-2-yl)-2-(p-tolyl)cyclobutyl)(phenyl)methanone **(3e)**

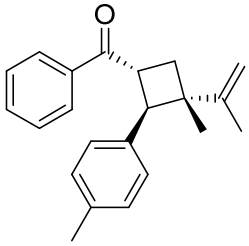


\+ diastereomers

3e (major)

3e (major) and diastereomers as a mixture: Yield (55.1 mg, 61%); Yellow liquid; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.92 (d, *J* = 7.3 Hz, 1.19H), 7.84 (d, *J* = 7.3 Hz, 0.54H), 7.79(d, *J* = 7.3 Hz,0.20H)7.53 (t, *J* = 7.4 Hz, 0.63H), 7.50 (d, *J* = 7.3 Hz, 0.45H), 7.42 (t, *J* = 7.7 Hz, 1.17H), 7.38 (t, *J* = 7.7 Hz, 0.72H), 7.11 – 7.14 (m, 1.73H), 7.06 – 7.09 (m, 1.70H), 7.04(d, *J* = 7.2 Hz,0.23H), 4.99(s, 0.07),4.98 (s, 0.24H), 4.91 (s, 0.34H), 4.89(s, 0.08),4.87 (s, 0.59H), 4.80 (s, 0.59H), 4.19 (q, *J* = 9.4 Hz, 0.63H), 4.09 (d, *J* = 9.7 Hz, 0.58H), 4.03 (q, *J* = 9.4Hz, 0.30H), 3.61 (d, *J* = 8.3 Hz, 0.30H), 2.76(t, *J* = 10.1 Hz, 0.44H), 2.36 (t, *J* = 10.1 Hz, 0.55H), 2.31 (s, 2.39H), 2.24 – 2.27 (m, 0.63H), 2.15 – 2.20 (m, 0.84H),1.76 (s, 0.28H), 1.73 (s, 1.87H), 1.38 (s, 0.91H), 1.15 (s, 1.83H), 1.12 (s, 0.99H).^{13}C NMR (150 MHz, $CDCl_3$) δ 200.4, 152.6, 148.5, 137.6, 136.9, 136.2, 135.8, 132.9, 132.9, 129.0, 129.0, 128.9, 128.8, 128.5, 128.5,

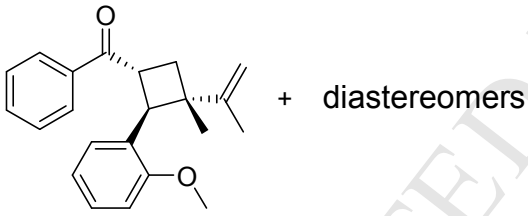
128.4, 128.4, 128.1, 127.9, 127.2, 110.6, 108.8, 52.9, 47.9, 46.8, 45.0, 42.5, 41.0, 36.2, 33.6, 28.7, 22.0, 21.0, 21.0, 20.1, 18.8.



3e

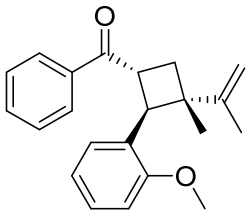
White solid, mp 107 – 109 ^{o}C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.98 (d, *J* = 7.4 Hz, 2H), 7.62 (t, *J* = 7.4 Hz, 1H), 7.50 (t, *J* = 7.7 Hz, 2H), 7.21 (d, *J* = 7.9 Hz, 2H), 7.10 (d, *J* = 7.8 Hz, 2H), 4.80 (s, 1H), 4.76 (s, 1H), 4.54 (q, *J* = 9.5 Hz, 1H), 3.83 (d, *J* = 9.8 Hz, 1H), 2.26 (s, 3H), 2.14 (d, *J* = 9.3 Hz, 2H), 1.67 (s, 3H), 1.08 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 200.8, 153.2, 136.9, 136.1, 135.8, 133.7, 129.2, 129.1, 128.8, 128.8, 108.8, 48.2, 45.0, 40.2, 35.8, 21.8, 21.1, 19.0. HRMS (ESI) calc. for $C_{22}H_{24}O$ $(M+Na)^+$: 327.1719, found: 327.1716.

4.2.6. (2-(2-methoxyphenyl)-3-methyl-3-(prop-1-en-2-yl)cyclobutyl)(phenyl)methanone **(3f)**



3f (major)

3f (major) and diastereomers as a mixture: Yield (47.1 mg, 49%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.91 (d, *J* = 7.1 Hz, 1.63H), 7.89 (d, *J* = 7.2 Hz, 0.27H), 7.51 (t, *J* = 7.4 Hz, 1.06H), 7.40 (t, *J* = 7.8 Hz, 2.01H), 7.26 (d, *J* = 7.5 Hz, 0.90H), 7.18 (d, *J* = 1.5Hz, 0.19H),7.17 (d, 7.9Hz, 0.80H), 6.91 (t, *J* = 7.4 Hz, 0.87H), 6.87 (t, *J* = 7.4 Hz, 0.17H), 6.79 (d, *J* = 8.2 Hz, 0.99H), 4.93 (s, 0.16H), 4.90 (s, 0.14H), 4.84 (s, 1.06H), 4.76 (s, 0.86H), 4.46 (d, *J* = 9.9 Hz, 0.83H), 4.28 (q, *J* = 9.4 Hz, 0.91H), 4.22 (d, *J* = 9.2 Hz, 0.14H), 4.15 (q, *J* =9.4 Hz, 0.18H), 3.77 (s, 0.39H), 3.62 (s, 2.66H), 2.73 (m, 0.17H), 2.44 (t, *J* = 10.0 Hz, 0.89H), 2.19 (m, 0.19H), 2.08 (m, 0.93H), 1.79 (s, 2.57H), 1.59(s, 0.38H),1.45 (s, 0.36H), 1.18 (s, 2.99H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 200.8, 200.6, 157.8, 157.7, 152.3, 148.6, 136.5, 136.3, 132.8, 132.8, 128.7, 128.5, 128.4, 128.4, 128.3, 128.3, 128.2, 127.6, 127.4, 127.4, 120.4, 120.2, 120.0, 110.6, 109.9, 108.3, 55.2, 54.9, 47.0, 45.5, 45.0, 42.5, 40.8, 40.6, 35.9, 34.4, 28.8, 21.9, 19.9, 18.9.

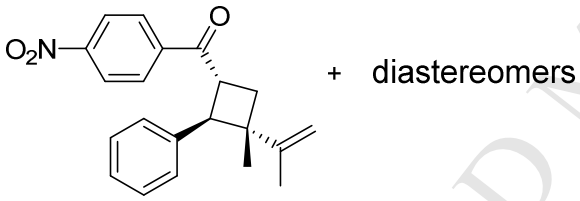


3f

Yellow liquid ; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.94 – 7.90 (m, 2H), 7.51 (t, *J* = 7.4 Hz, 1H), 7.40 (t, *J* = 7.8 Hz, 2H), 7.28 – 7.24 (m, 1H), 7.18 – 7.16 (m, 1H), 6.91 (t, *J* = 7.2 Hz, 1H), 6.79 (d, *J* = 8.2 Hz, 1H), 4.84 (s, 1H), 4.76 (s, 1H), 4.46 (d, *J* = 9.9 Hz, 1H), 4.28 (q, *J* = 9.4 Hz, 1H), 3.62 (s, 3H), 2.44 (t, *J* = 10.0 Hz, 1H), 2.09 – 2.07 (m, 1H), 1.79 (s, 3H), 1.18 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 200.6, 157.8, 152.3, 136.6, 132.7, 128.7, 128.5, 128.4, 128.3, 128.3, 127.4, 120.0, 110.6, 108.3, 54.9, 45.0, 42.6, 40.8, 35.9, 21.9, 18.9.

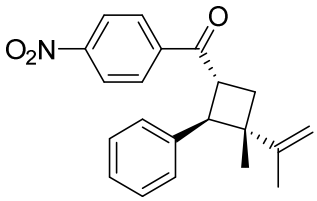
HRMS (ESI) calc. for $C_{22}H_{24}O_2$ $(M+Na)^+$: 343.1669, found: 343.1671

4.2.7. (3-methyl-2-phenyl-3-(prop-1-en-2-yl)cyclobutyl)(4-nitrophenyl)methanone **(3g)**



3g (major)

3g (major) and diastereomers as a mixture: Yield (26.7 mg, 27%); Yellow liquid ; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.25 (d, *J* = 8.8 Hz, 1.46H), 8.20 (d, *J* = 8.8 Hz, 0.53H), 8.03 (d, *J* = 8.8 Hz, 1.50H), 7.94 (d, *J* = 8.8 Hz, 0.52H), 7.34 – 7.27 (m, 2.07H), 7.25 – 7.22 (m, 2.62H), 5.01 (s, 0.25H), 4.95 (s, 0.26H), 4.88 (s, 0.73H), 4.83 (s, 0.74H), 4.20 (q, *J* = 9.4 Hz, 0.81H), 4.07 (d, *J* = 9.7 Hz, 0.77H), 4.06 – 4.02 (m, 0.31H), 3.57 (d, *J* = 8.4 Hz, 0.28H), 2.79 (dd, *J* = 11.9, 9.6 Hz, 0.31H), 2.45 – 2.42 (m, 0.77H), 2.33 (m, 0.34H), 2.22 – 2.16 (m, 0.82H), 1.73 (s, 2.25H), 1.40 (s, 0.77H), 1.18 (s, 2.26H), 1.10 (s, 0.78H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 199.0, 152.2, 150.3, 147.9, 140.6, 139.2, 129.4, 129.3, 128.3, 128.3, 128.2, 127.9, 127.1, 126.8, 123.8, 123.7, 111.1, 109.0, 53.8, 48.9, 47.0, 45.2, 43.0, 41.6, 35.6, 32.9, 28.7, 22.0, 20.0, 18.7.

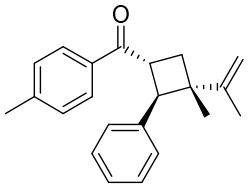


3g

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.24 (d, *J* = 8.8 Hz, 2H), 8.03 (d, *J* = 8.8 Hz, 2H), 7.34 – 7.29 (m, 2H), 7.26 – 7.21 (m, 3H), 4.88 (s, 1H), 4.83 (s, 1H), 4.20 (q, *J* = 9.4 Hz, 1H), 4.07 (d, *J* = 9.7 Hz, 1H), 2.45 – 2.42 (m, 1H), 2.22 – 2.17 (m, 1H), 1.73 (s, 3H), 1.18 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 199.0, 152.2, 140.6, 139.2, 129.3, 128.3, 128.2, 126.8, 123.8, 109.0, 48.9, 45.2, 41.6, 35.6, 22.0, 18.7.

HRMS (ESI) calc. for $C_{21}H_{21}NO_3$ $(M+Na)^+$: 358.1414, found: 358.1413.

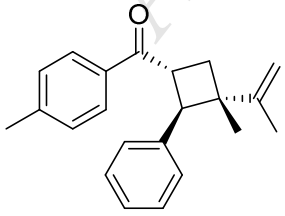
4.2.8. (3-methyl-2-phenyl-3-(prop-1-en-2-yl)cyclobutyl)(p-tolyl)methanone **(3h)**



+ diastereomers

3h (major)

3h (major) and diastereomers as a mixture: Yield (52.8 mg,58%); ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.89 (d, *J* = 8.0 Hz, 1.49H), 7.79 (d, *J* = 8.0 Hz, 0.36H), 7.69 (d, *J* = 8.0 Hz, 0.15H), 7.34 – 7.24 (m, 7.54H), 7.17 – 7.21 (m, 1.75H), 720 – 7.17(m, 0.29H), 5.04 (s, 0.20H), 4.98 (s, 0.08H), 4.86 (s, 0.16H), 4.84 (s, 0.08H), 4.82 (s, 0.74H), 4.77 (s, 0.76H), 4.53 (q, *J* = 9.5 Hz, 0.74H), 4.18 (q, *J* = 8.9 Hz, 0.22H), 3.89 (d, *J* = 9.8 Hz, 0.75H), 3.59 (d, *J* = 8.6 Hz, 0.21H), 2.36 – 2.34 (m, 2.71H),2.33(s, 0.29), 2.16 – 2.10 (m, 1.53H),2.05 – 2.02(m, 0.21), 1.70(s, 0.24), 1.68 (s, 2.24H), 1.32 (s, 0.54H), 1.09 (s, 2.22H), 1.06 (s, 0.58H).^{13}C NMR (150 MHz, DMSO-d_6) δ 200.3, 200.1, 153.1, 147.7, 144.1, 144.1, 140.8, 140.1, 133.6, 133.3, 129.7, 129.4, 128.9, 128.9, 128.8, 128.7, 128.4, 128.4, 128.2, 126.9, 126.8, 111.8, 108.9, 52.7, 48.4, 46.6, 45.0, 41.4, 36.0, 34.1, 28.9, 21.8, 21.6, 21.2, 20.4, 19.0.

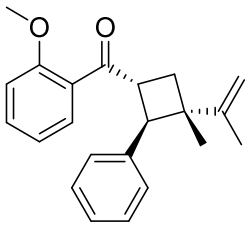


3h

White solid, mp 112 – 114 ^{o}C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.89 (d, *J* = 8.1 Hz, 2H), 7.34 –

7.27 (m, 6H), 7.22 – 7.19 (m, 1H), 4.82 (s, 1H), 4.77 (s, 1H), 4.54 (q, *J* = 9.5 Hz, 1H), 3.88 (d, *J* = 9.8 Hz, 1H), 2.36 (s, 3H), 2.16 – 2.10 (m, 2H), 1.68 (s, 3H), 1.09 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 200.3, 153.1, 144.1, 140.1, 133.6, 129.7, 128.9, 128.8, 128.5, 126.8, 108.9, 48.3, 45.0, 36.0, 21.8, 21.6, 19.1. HRMS (ESI) calc. for $C_{22}H_{24}O$ $(M+Na)^+$: 327.1719, found: 327.1718.

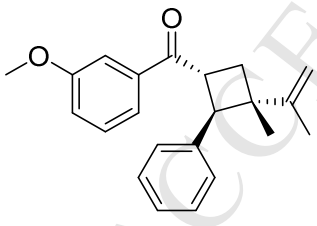
4.2.9. (2-methoxyphenyl)(3-methyl-2-phenyl-3-(prop-1-en-2-yl)cyclobutyl)methanone **(3i)**



3i

Yield (58.0 mg, 60%); Yellow liquid ; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.57 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.43 – 7.39 (m, 1H), 7.23 – 7.25 (m, 2H), 7.19 (d, *J* = 7.4 Hz, 2H), 7.16 (t, *J* = 7.2 Hz, 1H), 6.96 (t, *J* = 7.5 Hz, 1H), 6.90 (d, *J* = 8.3 Hz, 1H), 4.88 (s, 1H), 4.81 (s, 1H), 4.26 (q, *J* = 9.5 Hz, 1H), 4.09 (d, *J* = 9.9 Hz, 1H), 3.84 (s, 3H), 2.22 – 2.23 (m, 1H), 2.12 – 2.06 (m, 1H), 1.74 (s, 3H), 1.07 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 158.2, 152.7, 140.4, 132.98, 130.2, 128.1, 127.9, 126.0, 120.7, 111.3, 108.8, 55.5, 48.2, 44.6, 44.5, 35.9, 21.7, 18.9. HRMS (ESI) calc. for $C_{22}H_{24}O_2$ $(M+Na)^+$: 343.1669, found: 343.1671.

4.2.10. (3-methoxyphenyl)(3-methyl-2-phenyl-3-(prop-1-en-2-yl)cyclobutyl)methanone **(3j)**

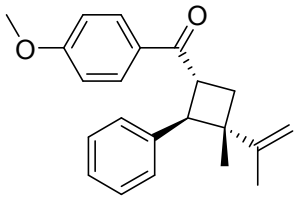


3j

Yield (51.8 mg, 54%); Yellow liquid ; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.51 (d, *J* = 7.7 Hz, 1H), 7.45 – 7.43 (m, 1H), 7.33 (t, *J* = 7.9 Hz, 1H), 7.29 (t, *J* = 7.5 Hz, 2H), 7.23 (d, *J* = 7.3 Hz, 2H), 7.20 (t, *J* = 7.2 Hz, 1H), 7.08 – 7.06 (m, 1H), 4.89 (s, 1H), 4.82 (s, 1H), 4.16 – 4.20 (m, 1H), 4.13 (d, *J* = 9.7 Hz, 1H), 3.78 (s, 3H), 2.41 – 2.37 (m, 1H), 2.19 – 2.15 (m, 1H), 1.74 (s, 3H), 1.15 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 200.2, 159.9, 152.5, 140.0, 137.6, 129.5, 128.2, 128.1, 126.4, 121.0, 119.6, 112.7,

108.9, 55.4, 48.2, 45.0, 41.1, 36.2, 22.0, 18.8. HRMS (ESI) calc. for $C_{22}H_{24}O_2$ $(M+Na)^+$: 343.1669, found: 343.1667

4.2.11. (4-methoxyphenyl)(3-methyl-2-phenyl-3-(prop-1-en-2-yl)cyclobutyl)methanone **(3k)**

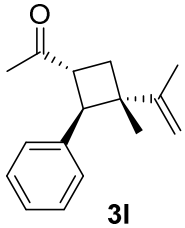


3k

Yield (43.1 mg, 45%); White solid, mp 96 – 98 ^oC; ^1H NMR (600 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.9 Hz, 2H), 7.28 (t, *J* = 7.5 Hz, 2H), 7.24 – 7.17 (m, 3H), 6.90 (d, *J* = 8.9 Hz, 2H), 4.89 (s, 1H), 4.81 (s, 1H), 4.19 – 4.13 (m, 2H), 3.85 (s, 3H), 2.35 (t, *J* = 9.8 Hz, 1H), 2.19 – 2.13 (m, 1H), 1.74 (s, 3H), 1.15 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 198.9, 163.5, 152.5, 140.1, 130.6, 128.1, 128.0, 126.2, 113.8, 108.8, 77.2, 77.0, 76.8, 55.40, 48.0, 45.0, 40.7, 36.4, 22.0, 18.8.

HRMS (ESI) calc. for $C_{22}H_{24}O_2$ $(M+Na)^+$: 343.1669, found: 343.1668.

4.2.12. 1-(3-methyl-2-phenyl-3-(prop-1-en-2-yl)cyclobutyl)ethan-1-one **(3l)**

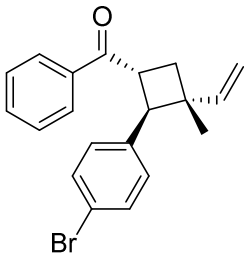


3l

Yield (27.8 mg, 41%); Yellowish oil; ^1H NMR (600 MHz, DMSO-d_6) δ 7.34 – 7.30 (m, 4H), 7.24-7.21 (m, 1H), 4.79 (s, 1H), 4.76 – 4.74 (m, 1H), 3.71 (m 1H), 3.61 (d, *J* = 10.3 Hz, 1H), 2.12 (t, *J* = 10.1 Hz, 1H), 1.98 (s, 3H), 1.89 (m, 1H), 1.67 (s, 3H), 0.94 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 209.1, 152.9, 139.8, 128.7, 128.5, 126.9, 109.0, 49.4, 44.4, 44.0, 33.2, 28.3, 21.6, 19.1.

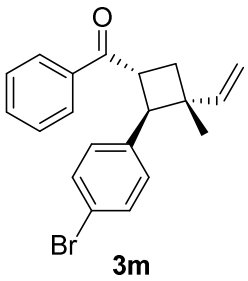
HRMS (ESI) calc. for $C_{16}H_{20}O$ $(M+Na)^+$: 251.1406, found: 251.1049.

4.2.13 (2-(4-bromophenyl)-3-methyl-3-vinylcyclobutyl)(phenyl)methanone (**3m**)



3m (major) + diastereomers

3h (major) and diastereomers as a mixture: Yield (57.6 mg, 54%); ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.96 (d, *J* = 8.4 Hz, 1.56H), 7.92 (d, *J* = 8.4 Hz, 0.39H), 7.75 – 7.72 (m, 1.84H), 7.66 (d, *J* = 8.3 Hz, 0.11H), 7.34 – 7.24 (m, 2.17H), 7.23 – 7.13 (m, 2.98H), 6.09 (dd, *J* = 17.2, 10.8 Hz, 0.81H), 5.84 – 5.80 (m, 0.20H), 5.05 (d, *J* = 17.4 Hz, 0.19H), 5.02 – 4.97 (m, 1.57H), 4.94 (d, *J* = 10.7 Hz, 0.19H), 4.62 (q, *J* = 9.6 Hz, 0.81H), 4.50 (q, *J* = 9.5 Hz, 0.21H), 3.80 (d, *J* = 10.0 Hz, 0.83H), 3.71 (d, *J* = 9.9 Hz, 0.20H), 2.45 (t, *J* = 10.0 Hz, 0.28H), 2.17 (t, *J* = 9.8 Hz, 0.80H), 2.10 (t, *J* = 10.0 Hz, 0.81H), 2.01 (t, *J* = 10.2 Hz, 0.26H), 1.31 (s, 0.51H), 0.96 (s, 2.39H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 200.1, 147.6, 143.1, 139.5, 135.0, 132.3, 130.9, 128.5, 128.4, 128.0, 127.9, 127.8, 126.7, 126.7, 112.8, 112.0, 51.7, 48.9, 43.2, 41.9, 40.6, 36.5, 35.6, 27.2, 20.6.



3m

White solid, mp 87 – 89 ^{o}C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.96 (d, *J* = 8.5 Hz, 2H), 7.74 (d, *J* = 8.5 Hz, 2H), 7.29 (t, *J* = 7.5 Hz, 2H), 7.21 – 7.17 (m, 3H), 6.09 (dd, *J* = 17.2, 10.8 Hz, 1H), 5.03 – 4.97 (m, 2H), 4.62 (q, *J* = 9.6 Hz, 1H), 3.80 (d, *J* = 10.0 Hz, 1H), 2.17 (t, *J* = 9.8 Hz, 1H), 2.10 (t, *J* = 10.0 Hz, 1H), 0.96 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 200.0, 147.6, 139.5, 135.0, 132.3, 130.9, 128.5, 127.8, 126.7, 112.0, 48.9, 41.9, 36.5, 20.6.

HRMS (ESI) calc. for $C_{20}H_{19}BrO$ $(M+H)^{+}$: 355.0692, found: 355.0696

ASSOCIATED CONTENT

Supporting Information

Preparation of starting materials, extra information for the optimization of reaction conditions,

optical spectroscopic data, olefins that resisted participating in the reaction with chalcone, computational methods, coordinates and energies, copies of ^{1}H NMR, ^{13}C NMR and HRMS spectra (PDF), and X-ray crystal structure of **3a** (CIF).

ACKNOWLEDGMENTS

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